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(54) Test card for performing assays

(57) An improved sample card is provided. The improved card, typically used in biochemical analysis, achieves high sample well capacity and improved fluid flow, including by means of a plurality of through-channels which route the fluid flow of samples along both the front and back surfaces of the card. Elevated bubble traps are provided, as are integral interrupt slots for sensing card position and alignment. A bezeled leading edge facilitates insertion.

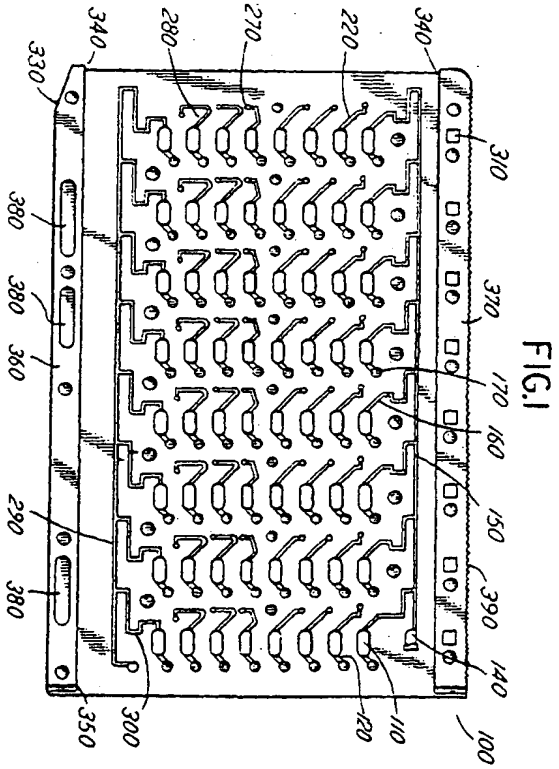

FIG.1

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shape and in standard dimensions. Biocard 100 in the illustrated embodiment contains a total of 64 separate sample wells 110, each of which receives a sample, for example a biological sample extracted from blood, other fluids, tissue or other material of a patient, for spectroscopic or other automated analysis. The biological sample may be a direct sample from the patient, or be patient sample which is extracted, diluted, suspended, or otherwise treated, in solution or otherwise. Other types of samples, including antibiotic dosages or other material, can also be introduced for analysis. It will be understood that well capacities other than 64 can be used. Biocard 100 is generally used in a landscape orientation.

In terms of materials, biocard 100 may be made of polystyrene, PET, or any other suitable plastic or other material. Biocard 100 may be tempered during manufacture with a softening material, so that crystalline rigidity, and resultant tendency to crack or chip, is reduced. Biocard 100 for instance may be manufactured out of a blend of polystyrene, approximately 90% or more, along with an additive of butyl rubber to render the card slightly more flexible and resistant to damage. Biocard 100 may also be doped with coloring agents, for instance titanium oxide to produce a white color, when desired.

The biocard 100 of the invention may be of use in identifying and/or enumerating any number of microorganisms, such as bacterial and/or other biological agents. Many bacteria lend themselves to automated spectroscopic, fluorescent and similar analysis after incubation, as is known in the art. The transmission and absorption of light is affected by the turbidity, density and colormetric properties of the sample. Fluorescent reactions may be performed as well, independently or along with spectroscopic or other measurements. If fluorescent data are gathered, use of a coloring agent in biocard 100 is preferable, since an opaque card reduces or eliminates the scattering of fluorescent emissions throughout the card, as can occur with a translucent material. Other types of detection and analysis can be done on biocard 100, including testing of susceptibility of microorganisms to antibiotics of different types, and at different concentrations, so that biocard 100 is a general-purpose instrument.

To receive sample fluid, the biocard 100 includes a sample intake plenum or port 120 at an upper right corner of the card 100, located on a perimeter edge of the card. The sample wells of card 100 contain dry biological reagents which are previously put in place in the wells, by evaporative, freeze-drying or other means, prior to being dissolved in solution with the injected patient sample for analysis. Each well can hold a deposit of a different reagent, for identifying different biological agents, if desired.

Intake port 120 receives a fluid injection tip and related assembly (schematically illustrated as 130), through which the sample fluid or other solution which arrives to dissolve the biological reagent is injected, under a vacuum pulled on biocard 100 (typically .7-.9 PSIA), then released to atmospheric pressure. Injection port 120 includes a small intake reservoir 140 formed as a roughly rectangular hole through the card 100, which receives incoming fluid, and acts as a fluid buffer.

The fluid (patient sample or other solution) enters intake port 120, collects in intake reservoir 140 and travels along first distribution channel 150, located on the front or facing side of card 100. First distribution channel 150 consists of a relatively long channel formed in the surface of card 100, which extends substantially across the width of the card, and may have a cross section of approximately .1-.2 mm^2. First distribution channel 150 is tapped at intervals along its length by a series of parallel distribution legs or fill channels 160, which generally descend from channel 150 toward the sample wells 110 in each of the eight illustrated columns. When the sample is injected into the card, a short segment of the sample tip can be pinched off or heat sealed and left in place in intake port 120, acting as a sealing plug.

Fill channels 160 are relatively short channels (which may be kinked) which extend down from first distribution channel 140 into respective sample wells 110 located in the first row of card 100, and having a cross section of approximately .1-.2 mm^2.

It will be appreciated that each of fill channels 160 descend to and enter sample wells 110 at an angle, which results in the natural flow of the sample fluid down through the fill channels 160 by gravity, and resistance to small pieces of undissolved material flowing back up into the fluid circuitry. When the sample fluid actually enters the well 110, the fluid fills the well by action of both gravity and a vortex-type of flow effect into that well. Also, any of the fill channels 160, as schematically illustrated in Figure 7, as well as other connecting fluid channels in the invention may be preferably formed in full-radius style, that is, as a semicircular conduit, rather than a squared-off channel as in some older designs. The full-radius feature has been found by the inventors to reduce friction and fluid turbulence, further enhancing the performance of biocard 100.

Each of sample wells 110 in the first and other rows includes an associated bubble trap 170, connected to sample well 110 at an upper corner of the well, and located at a height slightly above the well on the card surface. As illustrated in Figure 7, each bubble trap 170 is connected to its respective well by a short trap connecting conduit 180, formed as a hollow passage part-way into the card surface and forming a short conducting path for trapped gaseous bubbles which have been formed in, or communicated to, the well 110 during the injection operation, by bacterial or other biological reaction, or otherwise. Bubble trap 170 does not cut through the card completely, instead consisting of a depression or well of roughly cylindrical shape, with a rounded bottom contour, and a volume of approximately 4.2 cubic mm in the illustrated embodiment.

Because the bubble trap 170 is located at an ele-

that the possibility of inter-well contamination is reduced. The well-to-well distance in fact in the illustrated embodiment comes to approximately 35 mm, significantly more than the 12mm or so on many older card designs.

The inventors have also observed that the rate of inter-well contamination varies with the square of the linear distance, so the elongated fluid paths significantly enhance the integrity of readings on the card. Contamination itself is a function of sample mixing (density of solution falling out of wells) and liquid molecular diffusion, both of which are discouraged by the relatively fine channel cross-sections in many sections of the overall fluid circuit, as well as overall path length.

The contamination rate is also reduced by the fact that the volume of the channels along the fluid circuit varies slightly along the overall circuit travelled by a given sample. That is, the through-channels, the three main distribution channels and other segments of the paths have cross-sectional areas which, although all relatively fine, may differ slightly. The change in volume over the path tends to retard the progression of contamination, as do dog-legged or kinked sections of connecting conduits.

All these structural adaptations cooperate in reducing the rate of inter-well contamination in the biocard 100. The inventors have, as one indication of contamination management, measured the time required for test dye to infiltrate a neighboring well in conventional biocards and the card of the invention. Contamination in a conventional, low-capacity, non-through-body card has been observed in approximately 2-4 hours. In the biocard of the invention under similar conditions, in contrast, the contamination time has been observed at 16-18 hours.

Besides contamination kinematics, the upper-placed bubble traps 170 also more efficiently scrub the sample wells 110 of gas bubbles which form after the sample injection. Samples are typically injected as noted by evacuating the card, introducing fluid at the intake and then releasing the vacuum pull, so that the whole fluid circuitry returns to atmospheric pressure. Vacuum filling of the card may typically be done over a period of 3-60 seconds, slower rates helping to reduce the tendency of bubbles to form. Those bubbles can ruin sample readings, so reducing them results in a smoother, more efficient, higher-capacity yet more reliable biocard.

In addition, the improved fluid circuitry of biocard 100, including full-radius fill and other channels, generally narrower channels than older card designs, width-variation and other features result in a high capture percentage of sample intake actually reaching the sample wells 110, which the inventors have calculated at as high as 90-95%. This compares with a capture percent in the 80s for older card designs.

For mechanical interaction with the automated reading machine, biocard 100 may also be provided with a series of sensor stop holes 310, located along the bottommost edge of the card. Sensor stop holes 310, illustrated as regularly spaced, rectangular through-holes, permit associated photodetectors to detect when a biocard 100 mounted in a reading machine has come into proper alignment for optical reading. The sensor stop holes 310 are arranged in vertical register with the vertical columns of wells 110, so that the optical detection of the stop hole 310 corresponds exactly to positioning of the sample wells 110 before optical reading devices. Older biocards have been aligned by sensor holes which are formed not integrally with the card itself, but in carriages or other supports which are attached to the card at some point in the reading process, as for instance disclosed in U.S. Patent No. 4,118,280. These structures have however been prone to time-consuming maintenance, particularly requiring the mechanical calibration and lining up of the carriage with the cards, and photodetectors. Integral sensor stop holes 310 eliminate that type of difficulty.

The biocard 100 of the invention is formed in the illustrated embodiment, as shown in Figure 7, with a mold parting line 320 which is formed most of the way down into a sample well 110, toward the bottom of the card as opposing mold dies meet during manufacture. Older card designs often had the mold parting line, which forms a tiny lip in a fluid cavity, at an upper point (above midway) of the card. The upper mold parting lines could tend to induce annular bubble rings to form during filling, as well as reduce the efficiency of drying of antibiotics or other material during manufacturing. The use of a downward offset mold parting line 320 avoids these difficulties, as well as improving the efficiency of chemical or antibiotic dehydration during incubation, and may act as a slight aperture during light and fluorescence reading operations. As illustrated in Figure 7, the walls of the sample well, and other features, are usually formed at a slight angle or incline (typically 1-4°), as an artifact of conventional molding processes in which separating the molded part from opposing molding pieces is made easier with slight surface inclinations. The shifting of the mold parting line 320 to the bottom area of biocard 100 likewise results in a smaller inclined (roughly speaking, trapezoidal) area in the bottom of the sample well which can tend to trap material, slightly.

Another advantage of biocard 100 of the invention is that patient sample and other markings are not introduced directly on the card itself, in pre-formed segments, as for example shown in aforementioned U.S. Patent No. 4,116,775 and others. Those on-card stipplings and markings can contribute to debris, mishandling and other problems. In the invention, instead, the card may be provided with bar-coding or other data markings by adhesive media, but markings or preformed information segments are not necessary (though some could be imprinted if desired) and debris, mishandling, loss of surface area and other problems can be avoided.

stop hole by the said optical system permits accurate alignment of the said wells with the said optical system as the said sample card moves relative to the said optical system for reading of the said wells, preferably the said sample card further comprising a peripheral edge portion, the said at least one stop hole being located in the said peripheral edge portion, preferably the said wells being arranged in a plurality of columns, a sensor stop hole being placed in registry with each of the said columns of wells, preferably the said sample card further comprising a peripheral edge portion, the said columns of wells being equidistantly spaced from each other in an array of sample wells and the said sensor stop holes being positioned in the said peripheral edge portion equidistantly spaced from one another.

8. A sample card for use by a reading machine having a sample card transport system characterised in that it comprises:

a card body defining a top surface and a bottom surface, a fluid intake port and at least one edge region, the said body defining a plurality of sample wells placed between the said first and second end regions and the said first and second side regions, the said edge region having a knurled texture surface increasing the friction between the said sample card and the said transport system; preferably the said edge region comprising first and second edge regions parallel to each other between the said first and second end regions and disposed on opposite sides of the said card body, the said knurled texture region being disposed on the said first edge region and the said second edge region having a slanted portion at the intersection of the said second edge region with one of the said first and second end regions.

9. A sample card characterised in that it comprises:

a card body defining a top surface and a bottom surface, a fluid intake port and a plurality of sample wells placed between first and second end regions and first and second side regions; and

a fluid channel network comprising a first distribution channel in communication with the said fluid intake port and a second distribution channel connecting the said first distribution channel with at least two of the said plurality of sample wells;

the said first and second distribution channels having different cross-sectional areas, thereby inhibiting potential cross-contamination between the said wells.

10. A sample card characterised in that it comprises:

a card body defining a first surface and a second surface, a fluid intake port and a plurality of sample wells placed between first and second end regions and first and second side regions; and

a fluid channel network comprising a first distribution channel in communication with the said fluid intake port and a second distribution channel connecting the said first distribution channel with at least two of the said plurality of sample wells, the said first and second fluid channels being provided in a first surface of the said card;

the said fluid channel network further comprising a third distribution fluid channel in communication with the said fluid intake port, a fourth distribution channel connected to the said third fluid channel, and a through-card fluid channel connected to the said fourth fluid channel and linking the said fourth fluid channel with one of the said plurality of sample wells, the

said third and fourth fluid channels being provided in a second surface of the said card;

whereby the said first and second fluid channels in the said first surface of the said card and the said third and fourth fluid channels in the said second surface of the said card increase the separation distance between the said wells of the said card, thereby reducing the risk of contamination between the said wells;

preferably each of the said sample wells comprising a bubble trap connected thereto by a connecting conduit with the said connecting conduit formed in the said first surface of the said card, but not in the said second surface, the said bubble traps comprising one or more depressions in the said first surface of the said card extending part-way through the said card, the said bubble traps thereby formed being in an elevated position with respect to the said sample wells.

11. A sample card characterised in that it comprises:

a card body defining a first surface and a second surface, a fluid intake port and a plurality of sample wells disposed between the said first and second surfaces; and

a fluid channel network connecting the said fluid intake port to the said wells;

each of the said sample wells comprising a bubble trap connected thereto by a connecting conduit with the said connecting conduit formed in the said first surface of the said card, but not in the said second surface, the said bubble traps comprising one or more depressions in the said first surface of the said card extending part-way

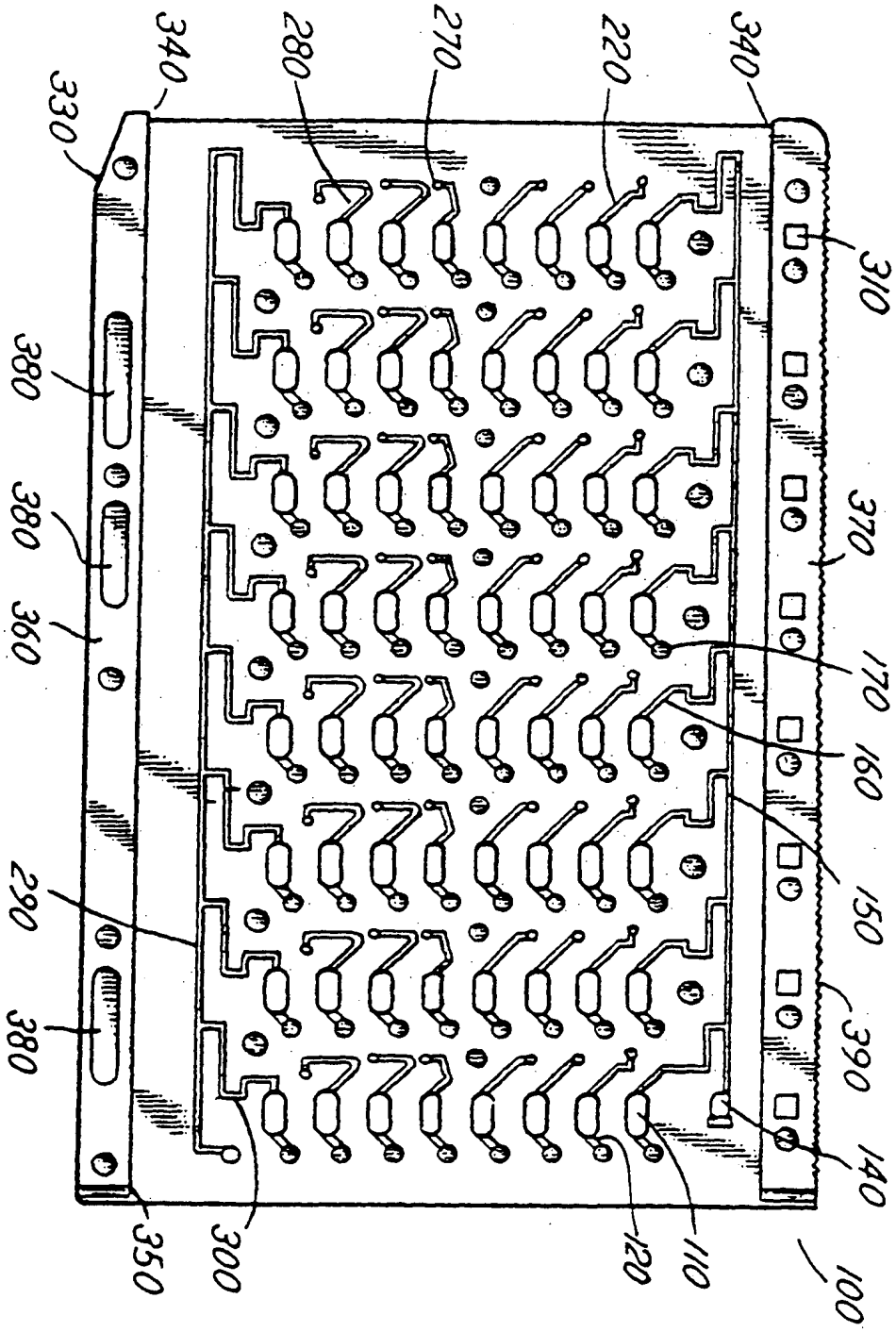
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FIG.1

FIG.3

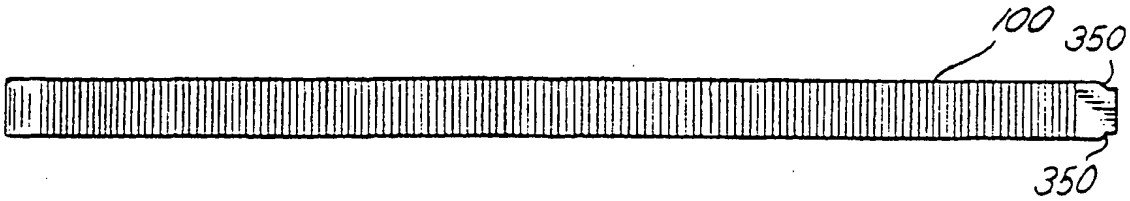


FIG.4

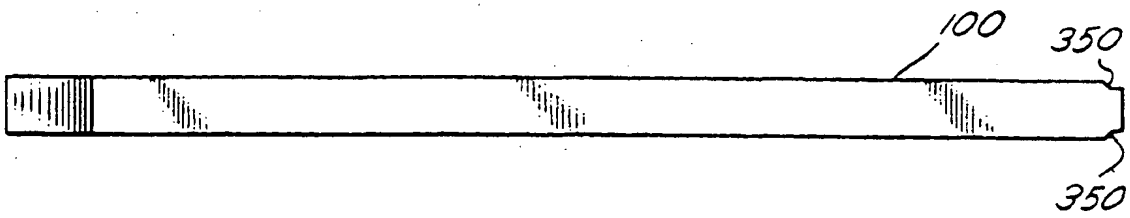


FIG.5

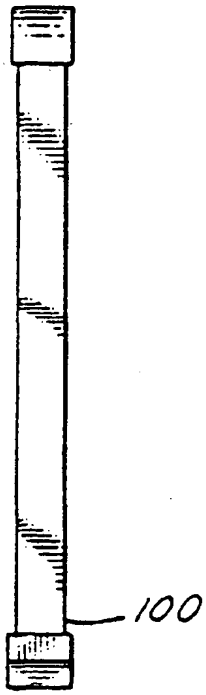
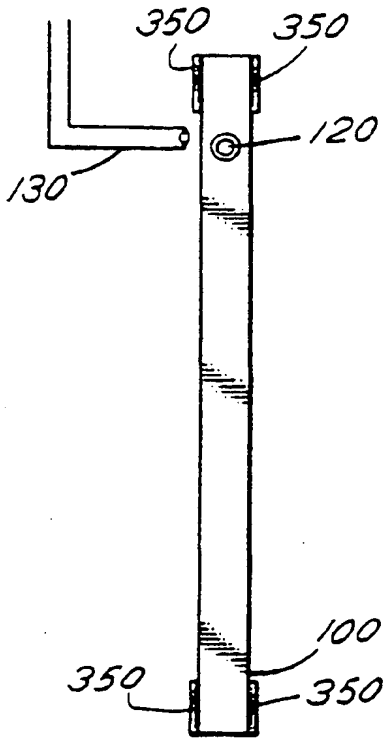


FIG.6



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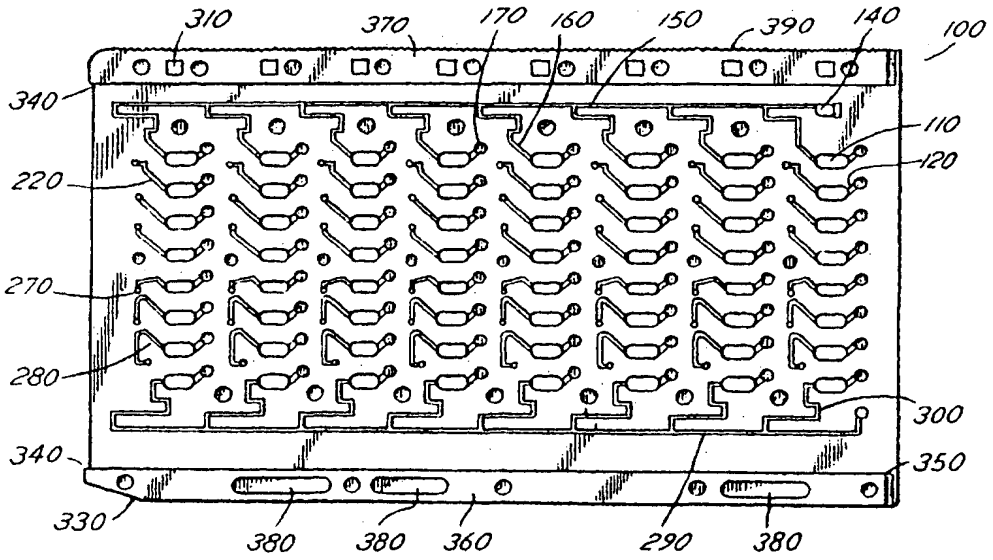
(54) Test card for performing assays

(57) An improved sample card (100) is provided. The improved card, typically used in biochemical analysis, achieves high sample well (110) capacity and improved fluid flow, including by means of a plurality of through-channels (150,160) which route the fluid flow of samples along both the front and back surfaces of the card (100). Elevated bubble traps (170) are provided, as are integral interrupt slots for sensing card position and alignment. A bezeled leading edge (330) facilitates insertion.

FIG.1



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EUROPEAN SEARCH REPORT

Application Number
EP 96 30 3457

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
X	US 4 018 652 A (LANHAM JAMES W ET AL)	11,13,14	
X	* column 3, line 47 - line 56; figure 4 *	11	
	* column 5, line 43 - line 49 *		
X	* column 7, line 54 - column 8, line 18 *	13	
	* column 12, line 44 - line 55 *		

A	US 4 116 775 A (CHARLES RONALD A ET AL)	13	
	* column 1, line 30 - line 43 *		
	* column 15, line 24 - line 54 *		

A	GB 2 025 611 A (SUOVANIEMI FINNPIPETTE)	7	
	* page 1, line 25 - line 54; claims 1,2,4,5 *		
	* page 1, line 100 - line 109 *		

A	US 4 395 125 A (KANEKO NOBUTAKA ET AL)	7	
	* column 1, line 30 - column 2, line 8; figures 1,2 *		

A	FR 2 368 774 A (ABBOTT LAB)	8,15,16	
	* page 1, line 21 - page 2, line 4 *		TECHNICAL FIELDS SEARCHED (Int.Cl.6)
A	* page 3, line 2 - line 5 *	8	
A	* page 3, line 5 - line 9; figures 2-5 *	15	
A	* page 3, line 23 - line 26; figure 6 *	7	

A	EP 0 445 053 A (GESPAC INSTR SA)	8	
	* column 3, line 39 - line 51; figures 8,9 *		

A	WO 83 03677 A (GENEFUSION SA)	8,13	
	* page 8, line 8 - page 9, line 7; figure 1 *		

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	12 December 1997	Hocquet, A

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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